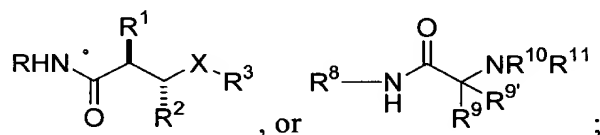


This listing of claims will replace all prior versions, and listings, of claims in the application.

Listing of Claims

1. **(currently amended)** A compound comprising:
 - i) 1-10 targeting moieties;
 - ii) a chelator; and
 - iii) 0-1 linking groups between the targeting moiety and chelator;wherein the targeting moiety is a matrix metalloproteinase inhibitor **having an inhibitory constant K_i of <100 nM**; and
wherein the chelator is capable of conjugating to a cytotoxic radioisotope.
2. **(cancelled)**
3. **(cancelled)**
4. **(original)** A compound according to claim 1, comprising 1-5 targeting moieties.
5. **(original)** A compound according to claim 1, comprising one targeting moiety.
6. **(currently amended)** A compound according to claim 1, wherein the targeting moiety is a matrix metalloproteinase inhibitor of the formulae (Ia) or (Ib):



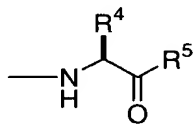
wherein,

R is independently OH or $-\text{CH}_2\text{SH}$;

R^1 is independently selected at each occurrence from the group: H, OH, C₁-3 alkyl, C₂-3 alkenyl, C₂-3 alkynyl, and heterocycle-S-CH₂-;

R^2 is independently C₁-20 alkyl;

X is independently C=O or SO₂, provided when X is C=O, R³ is



, and when X is SO₂, R³ is independently selected from the group: aryl substituted with 0-2 R⁶, and heterocycle substituted with 0-2 R⁶;

R⁴ is independently selected at each occurrence from the group: C₁₋₆ alkyl, phenyl, and benzyl;

R⁵ is independently selected at each occurrence from the group: NH(C₁₋₆ alkyl), NH-phenyl, and NH-heterocycle; wherein said alkyl, phenyl and heterocycle groups are optionally substituted with a bond to the linking group or a bond to the chelator;

R⁶ is independently aryloxy substituted with 0-3 R⁷;

R⁷ is independently halogen or methoxy;

or alternatively,

R¹ and R⁴ may be taken together to form a bridging group of the formula —(CH₂)₃-O-phenyl-CH₂—, optionally substituted with a bond to the linking group or a bond to the chelator;

or alternatively,

R¹ and R² may be taken together to form a bridging group of the formula —(CH₂)₃-NH—, optionally substituted with a bond to the linking group or a bond to the chelator; or

R¹ and R² taken together with the ~~nitrogen and~~ carbon ~~atom~~ atoms through which they are attached form a C₅₋₇ atom saturated ring system substituted with one or more substituents selected from the group consisting of: a bond to ~~Ln~~ said linking group, a bond to ~~Ch~~ said chelator, and —C(=O)-NR²⁹R³⁰;

R⁸ is independently at each occurrence OH or phenyl, optionally substituted with a bond to the linking group or a bond to the chelator, provided that when R⁸ is phenyl, R¹⁰ is —C(=O)-CR¹²-NH-CH(CH₃)-COOH— —C(=O)-CHR¹²-NH-CH(CH₃)-COOH;

R^9 and $R^{9'}$ are independently H, C₁₋₆ alkyl optionally substituted with a bond to the linking group or a bond to the chelator, or are taken together with the carbon atom to which R^9 and $R^{9'}$ are attached to form a 5-7 atom saturated, partially unsaturated or aromatic ring system containing 0-3 heteroatoms selected from O, N, SO₂ and S, said ring system substituted with R^6 and optionally substituted with a bond to the linking group or a bond to the chelator;

R^{10} and R^{11} are independently H, or C₁₋₆ alkyl optionally substituted with a bond to the linking group or a bond to the chelator, or are taken together with the nitrogen atom to which they are attached to form a 5-7 atom saturated, partially unsaturated or aromatic ring system containing 0-3 heteroatoms selected from O, N, SO₂ and S, said ring system optionally substituted with 0-3 R^{27} , a bond to the linking group or a bond to the chelator;

or alternatively,

R^9 and R^{10} are taken together with the nitrogen atom and carbon atom to which they are attached to form a 5-7 atom saturated, partially unsaturated or aromatic ring system containing ~~0-3~~ 0-2 additional heteroatoms selected from O, N, SO₂ and S, said ring system optionally substituted with a bond to the linking group or a bond to the chelator; and

R^{12} is independently C₁₋₂₀ alkyl;

R^{27} is =O, ~~C₁₋₄ alkyl~~ C₁₋₄ alkyl, or phenyl substituted with R^{28} ;

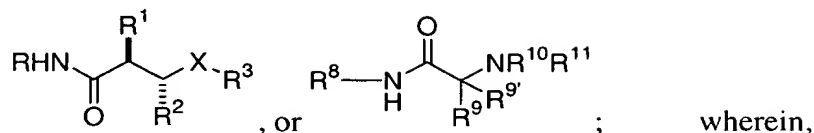
R^{28} is a phenoxy group substituted with 0-2 OCH₃ groups;

R^{29} and R^{30} taken together with the nitrogen atom through which they are attached form a ~~C₅₋₇~~ C₅₋₇ atom saturated ring system substituted with R^{31} ; and

R^{31} is a benzyloxy group substituted with ~~C₁₋₄ alkyl~~ C₁₋₄ alkyl.

7. (currently amended) A compound according to claim 1 ~~wherein~~

~~A compound according to claim 1~~, wherein the targeting moiety is a matrix metalloproteinase inhibitor of the formulae (Ia) or (Ib):

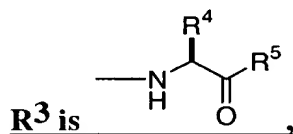


R is OH;

R¹ is independently selected at each occurrence from the group: H, OH, C₁₋₃ alkyl, C₂₋₃ alkenyl, C₂₋₃ alkynyl, and heterocycle-S-CH₂-;

R² is independently C₁₋₆ alkyl;

X is C=O;



R⁴ is independently selected at each occurrence from the group: C₁₋₆ alkyl, phenyl, and benzyl;

R⁵ is independently selected at each occurrence from the group: NH(C₁₋₆ alkyl), NH-phenyl, and NH-heterocycle; wherein said alkyl, phenyl and heterocycle groups are optionally substituted with a bond to the linking group or a bond to the chelator;

R⁶ is independently aryloxy substituted with 0-3 R⁷;

R⁷ is independently halogen or methoxy;

or alternatively,

R¹ and R⁴ may be taken together to form a bridging group of the formula -(CH₂)₃-O-phenyl-CH₂-, optionally substituted with a bond to the linking group or a bond to the chelator;

or alternatively,

R¹ and R² may be taken together to form a bridging group of the formula -(CH₂)₃-NH-, optionally substituted with a bond to the linking group or a bond to the chelator; or

R¹ and R² taken together with the ~~nitrogen and~~ carbon atom atoms through which they are attached form a C₅₋₇ atom saturated ring system substituted with one

or more substituents selected from the group consisting of: a bond to ~~Ln~~ said linking group, a bond to ~~Ch~~ said chelator, and $-C(=O)-NR^{29}R^{30}$;

R^8 is OH;

R^9 and $R^{9'}$ are independently H, C₁₋₆ alkyl optionally substituted with a bond to the linking group or a bond to the chelator, or are taken together with the carbon atom to which R^9 and $R^{9'}$ are attached to form a 5-7 atom saturated, partially unsaturated or aromatic ring system containing 0-1 heteroatoms selected from O, and N, $\bar{\gamma}$ said ring system optionally substituted with a bond to the linking group or a bond to the chelator;

R^{10} and R^{11} are independently H, or C₁₋₆ alkyl optionally substituted with a bond to the linking group or a bond to the chelator, or are taken together with the nitrogen atom to which they are attached to form a 5-7 atom saturated, partially unsaturated or aromatic ring system containing 0-1 heteroatoms selected from O, and N, $\bar{\gamma}$ said ring system optionally substituted with 0-3 R^{27} , a bond to the linking group or a bond to the chelator;

or alternatively,

R^9 and R^{10} are taken together with the nitrogen atom and carbon atom to which they are attached to form a 5-7 atom saturated, partially unsaturated or aromatic ring system containing an additional 0-1 heteroatoms heteroatom selected from O, and N, $\bar{\gamma}$ said ring system optionally substituted with a bond to the linking group or a bond to the chelator; and

R^{12} is independently C₁₋₆ alkyl;

R^{27} is =O, ~~C₁₋₄ alkyl~~ C₁₋₄ alkyl, or phenyl substituted with R^{28} ;

R^{28} is a phenoxy group substituted with 0-2 OCH₃ groups;

R^{29} and R^{30} taken together with the nitrogen atom through which they are attached form a C₅₋₇ atom saturated ring system substituted with R^{31} ; and

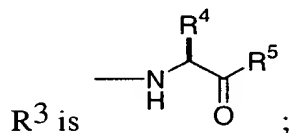
R^{31} is a benzyloxy group substituted with ~~C₁₋₄ alkyl~~ C₁₋₄ alkyl.

8. (currently amended) A compound according to claim 7 wherein:

R is -OH;

R² is C₁₋₆ alkyl;

X is C=O;



R¹ and R⁴ are taken together to form a bridging group of formula -(CH₂)₃-O-phenyl-CH₂-;

R⁵ is ~~NH(C₁₋₆alkyl)~~, NH(C₁₋₆alkyl), substituted with a bond to the linking group or a bond to the chelator.

9. (*currently amended*) A compound according to claim 7, wherein:

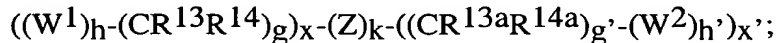
R is -OH;

R¹ and R² taken together with the ~~nitrogen and~~ carbon ~~atom~~ atoms through which they are attached form a C₅₋₇ atom saturated ring system substituted with one or more substituents selected from the group consisting of: a bond to ~~Ln~~ said linking group, a bond to ~~Ch~~ said chelator, and -C(=O)-NR²⁹R³⁰;

R²⁹ and R³⁰ taken together with the nitrogen atom through which they are attached form a ~~C₅₋₇~~ C₅₋₇ atom saturated ring system substituted with R³¹; and

R³¹ is a benzyloxy group substituted with ~~C₁₋₄alkyl~~ C₁₋₄ alkyl.

10. (*currently amended*) A compound according to claim 1, wherein the linking group is of the formula:



W¹ and W² are independently selected at each occurrence from the group: O, S, NH, NHC(=O), C(=O)NH, NR¹⁵C(=O), C(=O)NR¹⁵, C(=O), C(=O)O, OC(=O), NHC(=S)NH, NHC(=O)NH, SO₂, SO₂NH, -(OCH₂CH₂)₇₆₋₈₄, (OCH₂CH₂)_s, (CH₂CH₂O)_{s'}, (OCH₂CH₂CH₂)_{s''}, (CH₂CH₂CH₂O)_t, and (aa)_{t'};

aa is independently at each occurrence an amino acid;

Z is selected from the group: aryl substituted with 0-3 R¹⁶, C₃₋₁₀ cycloalkyl substituted with 0-3 R¹⁶, and a 5-10 membered heterocyclic ring system containing 1-4 heteroatoms independently selected from N, S, and O and substituted with 0-3 R¹⁶;

R¹³, R^{13a}, R¹⁴, R^{14a}, and R¹⁵ are independently selected at each occurrence from the group: H, =O, COOH, SO₃H, PO₃H, C₁₋₅ alkyl substituted with 0-3 R¹⁶, aryl substituted with 0-3 R¹⁶, benzyl substituted with 0-3 R¹⁶, and C₁₋₅ alkoxy substituted with 0-3 R¹⁶, NHC(=O)R¹⁷, C(=O)NHR¹⁷, NHC(=O)NHR¹⁷, NHR¹⁷, R¹⁷, and a bond to the chelator;

R¹⁶ is independently selected at each occurrence from the group: a bond to the chelator, COOR¹⁷, C(=O)NHR¹⁷, NHC(=O)R¹⁷, OH, NHR¹⁷, SO₃H, PO₃H, -OPO₃H₂, -OSO₃H, aryl substituted with 0-3 R¹⁷, C₁₋₅ alkyl substituted with 0-1 R¹⁸, C₁₋₅ alkoxy substituted with 0-1 R¹⁸, and a 5-10 membered heterocyclic ring system containing 1-4 heteroatoms independently selected from N, S, and O and substituted with 0-3 R¹⁷;

R¹⁷ is independently selected at each occurrence from the group: H, alkyl substituted with 0-1 R¹⁸, aryl substituted with 0-1 R¹⁸, a 5-10 membered heterocyclic ring system containing 1-4 heteroatoms independently selected from N, S, and O and substituted with 0-1 R¹⁸, C₃₋₁₀ cycloalkyl substituted with 0-1 R¹⁸, polyalkylene glycol substituted with 0-1 R¹⁸, carbohydrate substituted with 0-1 R¹⁸, cyclodextrin substituted with 0-1 R¹⁸, amino acid substituted with 0-1 R¹⁸, polycarboxyalkyl substituted with 0-1 R¹⁸, polyazaalkyl substituted with 0-1 R¹⁸, peptide substituted with 0-1 R¹⁸, wherein the peptide is comprised of 2-10 amino acids, 3,6-O-disulfo-B-D-galactopyranosyl, bis(phosphonomethyl)glycine, and a bond to the chelator;

R¹⁸ is a bond to the chelator;

k is selected from 0, 1, and 2;

h is selected from 0, 1, and 2;
h' is selected from 0, 1, and 2;
g is selected from 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, and 10;
g' is selected from 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, and 10;
s is selected from 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, and 10;
s' is selected from 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, and 10;
s'' is selected from 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, and 10;
t is selected from 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, and 10;
t' is selected from 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, and 10;
x is selected from 0, 1, 2, 3, 4, and 5; and
x' is selected from 0, 1, 2, 3, 4, and 5.

11. (*currently amended*) A compound according to claim 10 wherein

W¹ and W² are independently selected at each occurrence from the group:
O, NH, NHC(=O), C(=O)NH, NR¹⁵C(=O), C(=O)NR¹⁵, C(=O), C(=O)O, OC(=O),
NHC(=S)NH, NHC(=O)NH, SO₂, -(CH₂CH₂O)₇₆₋₈₄-, (OCH₂CH₂)_s,
(CH₂CH₂O)_s', (OCH₂CH₂CH₂)_s'', (CH₂CH₂CH₂O)_t, and (aa)_t';

aa is independently at each occurrence an amino acid;

Z is selected from the group: aryl substituted with 0-1 R¹⁶, C₃₋₁₀ cycloalkyl substituted with 0-1 R¹⁶, and a 5-10 membered heterocyclic ring system containing 1-4 heteroatoms independently selected from N, S, and O and substituted with 0-1 R¹⁶;

R¹³, R^{13a}, R¹⁴, R^{14a}, and R¹⁵ are independently selected at each occurrence from the group: H, =O, COOH, SO₃H, C₁-C₅ alkyl substituted with 0-1 R¹⁶, aryl substituted with 0-1 R¹⁶, benzyl substituted with 0-1 R¹⁶, **and** C₁-C₅ alkoxy substituted with 0-1 R¹⁶, NHC(=O)R¹⁷, C(=O)NHR¹⁷, NHC(=O)NHR¹⁷, NHR¹⁷, R¹⁷, and a bond to the chelator;

k is 0 or 1;

s is selected from 0, 1, 2, 3, 4, and 5;

s' is selected from 0, 1, 2, 3, 4, and 5;
s'' is selected from 0, 1, 2, 3, 4, and 5; and
t is selected from 0, 1, 2, 3, 4, and 5.

12. *(original)* A compound according to claim 10, wherein:

W¹ is C(=O)NR¹⁵;
h is 1;
g is 3;
R¹³ and R¹⁴ are independently H;
x is 1;
k is 0;
g' is 0;
h' is 1;
W² is NH; and
x' is 1.

13. *(original)* A compound according to claim 10, wherein:

x is 0;
k is 1;
Z is aryl substituted with 0-3 R¹⁶;
g' is 1;
W² is NH;
R^{13a} and R^{14a} are independently H;
h' is 1; and
x' is 1.

14. *(original)* A compound according to claim 10, wherein:

W¹ is C(=O)NR¹⁵;
h is 1;
g is 2;

R¹³ and R¹⁴ are independently H;
x is 1;
k is 0;
g' is 1;
R^{13a} and R^{14a} are independently H; or C₁₋₅ alkyl substituted with 0-3 R¹⁶;
R¹⁶ is SO₃H;
W² is NHC(=O) or NH;
h' is 1; and
x' is 2.

15. *(original)* A compound according to claim 10, wherein:

W¹ is C(=O)NH;
h is 1;
g is 3;
R¹³ and R¹⁴ are independently H;
k is 0;
g' is 0;
x is 1;
W² is -NH(C=O)- or -(OCH₂CH₂)₇₆₋₈₄;
h' is 2; and
x' is 1.

16. *(original)* A compound according to claim 10, wherein:

x is 0;
k is 0;
g' is 3;
h' is 1;
W² is NH; and
x' is 1.

17. *(currently amended)* A compound according to claim 10, wherein:

x is 0;

Z is aryl substituted with 0-3 R¹⁶;

k is 1;

g' is 1;

R^{13a} and R^{14a} are independently H;

W² is NHC(=O) or ~~-(OCH₂CH₂)₇₆₋₈₄-~~ -(OCH₂CH₂)₇₆₋₈₄-; and

x' is 1.

18. *(original)* A compound according to claim 10, wherein:

W¹ is C=O;

g is 2;

R¹³ and R¹⁴ are independently H;

k is 0;

g' is 0;

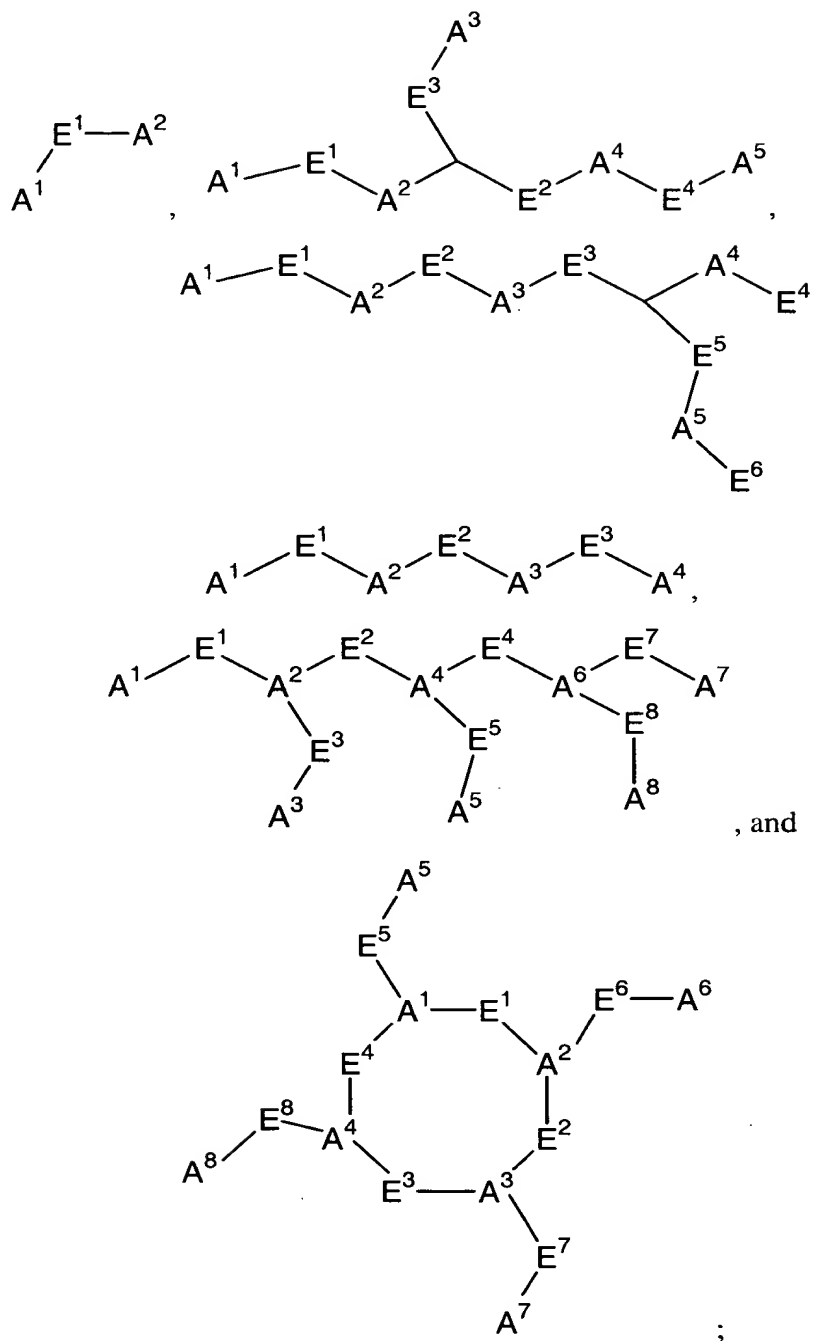
h' is 1;

W² is NH; and

x' is 1.

19. *(original)* A compound according to claim 1 wherein the linking group is absent.

20. *(original)* A compound according to claim 1, wherein the chelator is a metal bonding unit having a formula selected from the group:



A^1 , A^2 , A^3 , A^4 , A^5 , A^6 , A^7 , and A^8 are independently selected at each occurrence from the group: N, NR^{26} , NR^{19} , $NR^{19}R^{20}$, S, SH, $-S(Pg)$, O, OH, PR^{19} , $PR^{19}R^{20}$, $-O-P(O)(R^{21})-O-$, $P(O)R^{21}R^{22}$, a bond to the targeting moiety and a bond to the linking group;

Pg is a thiol protecting group;

E¹, E², E³, E⁴, E⁵, E⁶, E⁷, and E⁸ are independently a bond, CH, or a spacer group independently selected at each occurrence from the group: C₁-C₁₆ alkyl substituted with 0-3 R²³, aryl substituted with 0-3 R²³, C₃-C₁₀ cycloalkyl substituted with 0-3 R²³, heterocyclo-C₁-C₁₀ alkyl substituted with 0-3 R²³, wherein the heterocyclo group is a 5-10 membered heterocyclic ring system containing 1-4 heteroatoms independently selected from N, S, and O, C₆-C₁₀ aryl-C₁-C₁₀ alkyl substituted with 0-3 R²³, C₁-C₁₀ alkyl-C₆-C₁₀ aryl- substituted with 0-3 R²³, and a 5-10 membered heterocyclic ring system containing 1-4 heteroatoms independently selected from N, S, and O and substituted with 0-3 R²³;

R¹⁹ and R²⁰ are each independently selected from the group: a bond to the linking group, a bond to the targeting moiety, hydrogen, C₁-C₁₀ alkyl substituted with 0-3 R²³, aryl substituted with 0-3 R²³, C₁-C₁₀ cycloalkyl substituted with 0-3 R²³, heterocyclo-C₁-C₁₀ alkyl substituted with 0-3 R²³, wherein the heterocyclo group is a 5-10 membered heterocyclic ring system containing 1-4 heteroatoms independently selected from N, S, and O, C₆-C₁₀ aryl-C₁-C₁₀ alkyl substituted with 0-3 R²³, C₁-C₁₀ alkyl-C₆-C₁₀ aryl- substituted with 0-3 R²³, a 5-10 membered heterocyclic ring system containing 1-4 heteroatoms independently selected from N, S, and O and substituted with 0-3 R²³, and an electron, provided that when one of R¹⁹ or R²⁰ is an electron, then the other is also an electron;

R²¹ and R²² are each independently selected from the group: a bond to the linking group, a bond to the targeting moiety, -OH, C₁-C₁₀ alkyl substituted with 0-3 R²³, C₁-C₁₀ alkyl substituted with 0-3 R²³, aryl substituted with 0-3 R²³, C₃-C₁₀ cycloalkyl substituted with 0-3 R²³, heterocyclo-C₁-C₁₀ alkyl substituted with 0-3 R²³, wherein the heterocyclo group is a 5-10 membered heterocyclic ring system containing 1-4 heteroatoms independently selected from N, S, and O, C₆-C₁₀ aryl-C₁-C₁₀ alkyl substituted with 0-3 R²³, C₁-C₁₀ alkyl-C₆-C₁₀ aryl- substituted with

0-3 R²³, and a 5-10 membered heterocyclic ring system containing 1-4 heteroatoms independently selected from N, S, and O and substituted with 0-3 R²³;

R²³ is independently selected at each occurrence from the group: a bond to the linking group, a bond to the targeting moiety, =O, F, Cl, Br, I, -CF₃, -CN, -CO₂R²⁴, -C(=O)R²⁴, -C(=O)N(R²⁴)₂, -CHO, -CH₂OR²⁴, -OC(=O)R²⁴, -OC(=O)OR^{24a}, -OR²⁴, -OC(=O)N(R²⁴)₂, -NR²⁵C(=O)R²⁴, -NR²⁵C(=O)OR^{24a}, -NR²⁵C(=O)N(R²⁴)₂, -NR²⁵SO₂N(R²⁴)₂, -NR²⁵SO₂R^{24a}, -SO₃H, -SO₂R^{24a}, -SR²⁴, -S(=O)R^{24a}, -SO₂N(R²⁴)₂, -N(R²⁴)₂, -NHC(=S)NHR²⁴, =NOR²⁴, NO₂, -C(=O)NHOR²⁴, -C(=O)NHN(R²⁴)R^{24a}, -OCH₂CO₂H, 2-(1-morpholino)ethoxy, C₁-C₅ alkyl, C₂-C₄ alkenyl, C₃-C₆ cycloalkyl, C₃-C₆ cycloalkylmethyl, C₂-C₆ alkoxyalkyl, aryl substituted with 0-2 R²⁴, and a 5-10 membered heterocyclic ring system containing 1-4 heteroatoms independently selected from N, S, and O; and

wherein at least one of A¹, A², A³, A⁴, A⁵, A⁶, A⁷, A⁸ or R²³ is a bond to the linking group or targeting moiety;

R²⁴, R^{24a}, and R²⁵ are independently selected at each occurrence from the group: a bond to the linking group, a bond to the targeting moiety, H, C₁-C₆ alkyl, phenyl, benzyl, C₁-C₆ alkoxy, halide, nitro, cyano, and trifluoromethyl; and

R²⁶ is a co-ordinate bond to a metal or a hydrazine protecting group.

21. (*currently amended*) A compound according to claim 20 wherein:

A¹, A², A³, A⁴, A⁵, A⁶, A⁷, and A⁸ are independently selected at each occurrence from the group: NR¹⁹, NR¹⁹R²⁰, S, SH, OH, a bond to the targeting moiety and a bond to the linking group;

E¹, E², E³, E⁴, E⁵, E⁶, E⁷, and E⁸ are independently a bond, CH, or a spacer group independently selected at each occurrence from the group: C₁-C₁₀ alkyl substituted with 0-3 R²³, aryl substituted with 0-3 R²³, C₃-₁₀ cycloalkyl substituted with 0-3 R²³, and a 5-10 membered heterocyclic ring system containing 1-4 heteroatoms independently selected from N, S, and O and substituted with 0-3 R²³;

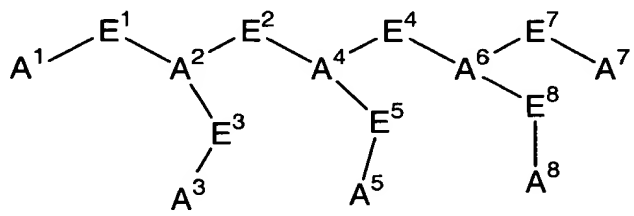
wherein at least one of A¹, A², A³, A⁴, A⁵, A⁶, A⁷, A⁸ and R²³ is a bond to the linking group or a targeting moiety;

R¹⁹, and R²⁰ are each independently selected from the group: a bond to the targeting moiety, a bond to the linking group, hydrogen, C₁-C₁₀ alkyl substituted with 0-3 R²³, aryl substituted with 0-3 R²³, a 5-10 membered heterocyclic ring system containing 1-4 heteroatoms independently selected from N, S, and O and substituted with 0-3 R²³, and an electron, provided that when one of R¹⁹ or R²⁰ is an electron, then the other is also an electron;

R²³ is independently selected at each occurrence from the group: a bond to the targeting moiety, a bond to the linking group, =O, F, Cl, Br, I, -CF₃, -CN, -CO₂R²⁴, -C(=O)R²⁴, -C(=O)N(R²⁴)₂, -CH₂OR²⁴, -OC(=O)R²⁴, -OC(=O)OR^{24a}, -OR²⁴, -OC(=O)N(R²⁴)₂, -NR²⁵C(=O)R²⁴, -NR²⁵C(=O)OR^{24a}, -NR²⁵C(=O)N(R²⁴)₂, -NR²⁵SO₂N(R²⁴)₂, -NR²⁵SO₂R^{24a}, -SO₃H, -SO₂R^{24a}, -S(=O)R^{24a}, -SO₂N(R²⁴)₂, -N(R²⁴)₂, -NHC(=S)NHR²⁴, ~~=NOR¹⁸,~~
~~-C(=O)NHNOR¹⁸R^{18a},~~ =NOR²⁴, -C(=O)NHNOR²⁴R^{24a}, -OCH₂CO₂H, and 2-(1-morpholino)ethoxy; and

R²⁴, R^{24a}, and R²⁵ are independently selected at each occurrence from the group: a bond to the linking group, H, and C₁-C₆ alkyl.

22. (*currently amended*) A compound according to claim 20 wherein the chelator is of the formula:



A¹ is a bond to the linking group;

A², A⁴, and A⁶ are each N;

A³, A⁵, A⁷ and A⁸ are each OH;

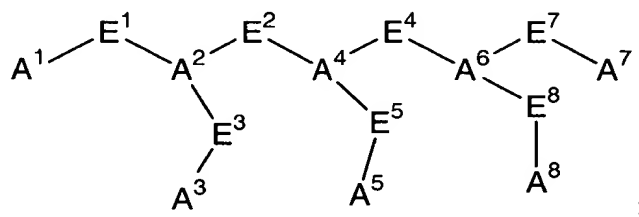
E¹, E², and E⁴ are ~~C₂ alkyl~~ C₂ alkyl;

E³, E⁵, E⁷, and E⁸ are C₂ alkyl substituted with 0-1 R²³; and

R²³ is =O;

23. (*currently amended*) A compound according to claim 20 wherein the chelator is of the formula:

Ch Ch is



wherein:

A₅ is a bond to Ln;

A¹, A³, A⁷ and A⁸ are each OH;

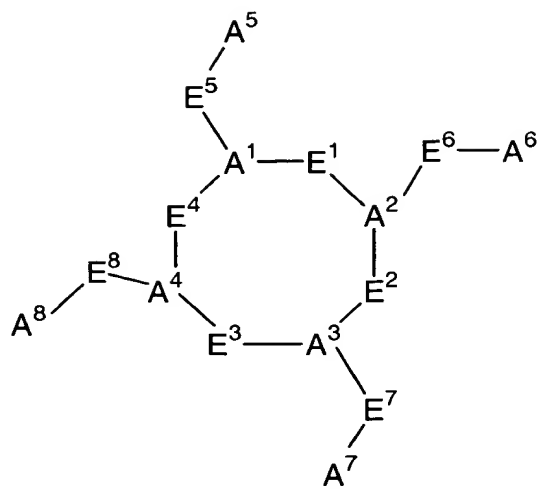
A², A⁴ and A⁶ are each NH;

E¹, E³, E⁵, E⁷, and E⁸ are C₂ alkyl substituted with 0-1 R²³;

E², and E⁴, are C₂ alkyl;

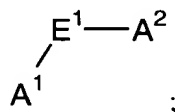
R²³ is =O.

24. (*currently amended*) A compound according to claim 20 wherein the chelator is of the formula:



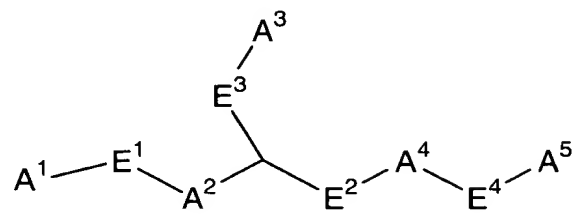
A¹, A², A³ and A⁴ are each N;
 A⁵, A⁶ and A⁸ are each OH;
 A⁷ is a bond to ~~Ln~~ said linking group;
 E¹, E², E³, E⁴ are each independently C₂ alkyl; and
 E⁵, E⁶, E⁷, E⁸ are each independently C₂ alkyl substituted with 0-1 R²³;
 R²³ is =O.

25. (*original*) A compound according to claim 20 wherein the chelator is of the formula:



A¹ is NR²⁶;
 R²⁶ is a co-ordinate bond to a metal or a hydrazine protecting group;;
 E¹ is a bond;
 A² is NHR¹⁹;
 R¹⁹ is a heterocycle substituted with R²³, the heterocycle being selected from pyridine and pyrimidine;
 R²³ is selected from a bond to the linking group, C(=O)NHR²⁴ and C(=O)R²⁴; and
 R²⁴ is a bond to the linking group.

26. (*currently amended*) A compound according to claim 20 wherein the chelator is of the formula:



wherein:

A¹ and A⁵ are each -S(Pg);

Pg is a thiol protecting group;

E¹ and E⁴ are C₂ alkyl substituted with 0-1 R²³;

R²³ is =O;

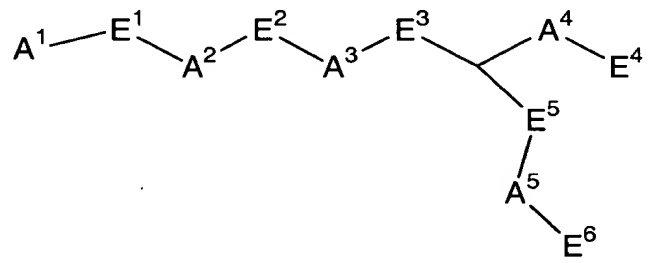
A² and A⁴ are each -NH;

E² is CH₂;

E³ is C₁₋₃ alkyl substituted with 0-1 R²³;

A³ is a bond to ~~L_n~~ said linking group.

27. (*original*) A compound according to claim 20 wherein the chelator is of the formula:



wherein:

A¹ is a bond to L_n;

E¹ is C₁ alkyl substituted by R²³;

A² is NH;

E² is C₂ alkyl substituted with 0-1 R²³;

A³ is -O-P(O)(R²¹)-O;

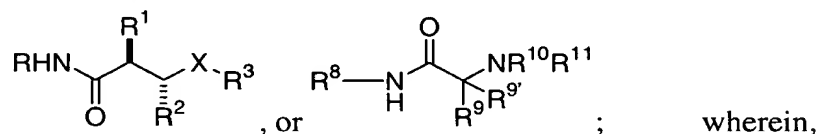
E³ is C₁ alkyl;

A^4 and A^5 are each $-O-$;
 E^4 and E^6 are each independently C_{1-16} alkyl substituted with 0-1 R^{23} ;
 E^5 is C_1 alkyl;
 R^{21} is $-OH$; and
 R^{23} is $=O$.

28. (currently amended) A compound of claim 1 having the formula:



wherein, L_n is said linking group, Ch is said chelator, and Q is a compound of Formulae (Ia) or (Ib):

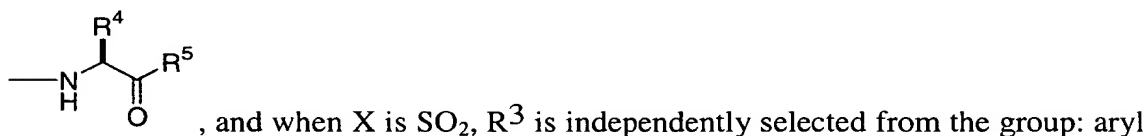


R is independently OH or $-CH_2SH$;

R^1 is independently selected at each occurrence from the group: H , OH , C_{1-3} alkyl, C_{2-3} alkenyl, C_{2-3} alkynyl, and heterocycle- $S-CH_2-$;

R^2 is independently C_{1-20} alkyl;

X is independently $C=O$ or SO_2 , provided when X is $C=O$, R^3 is



substituted with 0-2 R^6 , and heterocycle substituted with 0-2 R^6 ;

R^4 is independently selected at each occurrence from the group: C_{1-6} alkyl, phenyl, and benzyl;

R^5 is independently selected at each occurrence from the group: $NH(C_{1-6}$ alkyl), NH -phenyl, and NH -heterocycle; wherein said alkyl, phenyl and heterocycle groups are optionally substituted with a bond to L_n ;

R^6 is independently aryloxy substituted with 0-3 R^7 ;

R^7 is independently halogen or methoxy;

or alternatively,

R¹ and R⁴ may be taken together to form a bridging group of the formula $-(CH_2)_3-O-phenyl-CH_2-$, optionally substituted with a bond to L_n; or alternatively,

R¹ and R² may be taken together to form a bridging group of the formula $-(CH_2)_3-NH-$, optionally substituted with a bond to L_n; or

R¹ and R² taken together with the ~~nitrogen and~~ carbon ~~atom~~ atoms through which they are attached form a C₅₋₇ atom saturated ring system substituted with one or more substituents selected from the group consisting of: a bond to L_n, a bond to Ch, and $-C(=O)-NR^{29}R^{30}$;

R⁸ is independently at each occurrence OH or phenyl, optionally substituted with a bond to L_n, provided that when R⁸ is phenyl, R¹⁰ is ~~$-C(=O)-CR^{12}-NH-CH(CH_3)-COOH$~~ $-C(=O)-CHR^{12}-NH-CH(CH_3)-COOH$;

R⁹ and R^{9'} are independently H, C₁₋₆ alkyl optionally substituted with a bond to L_n, or are taken together with the carbon atom to which they are attached to form a 5-7 atom saturated, partially unsaturated or aromatic ring system containing 0-3 heteroatoms selected from O, N, SO₂ and S, said ring system substituted with R⁶ and optionally substituted with a bond to ~~L_n~~ L_n;

R¹⁰ and R¹¹ are independently H, or C₁₋₆ alkyl optionally substituted with a bond to ~~L_n~~ L_n, or are taken together with the nitrogen atom to which they are attached to form a 5-7 atom saturated, partially unsaturated or aromatic ring system containing 0-3 heteroatoms selected from O, N, SO₂ and S, said ring system optionally substituted with 0-3 R²⁷ or a bond to ~~L_n~~ L_n;

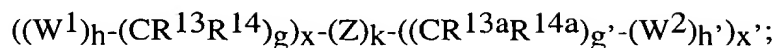
or alternatively,

R⁹ and R¹⁰ are taken together with the nitrogen atom and carbon atom to which they are attached to form a 5-7 atom saturated, partially unsaturated or aromatic ring system containing ~~0-3~~ 0-2 additional heteroatoms selected from O, N, SO₂ and S, said ring system optionally substituted with a bond to ~~L_n~~ L_n;

R¹² is independently C₁₋₂₀ alkyl;

d is selected from 1, 2, 3, 4, 5, 6, 7, 8, 9, and 10;

L_n L_n is a linking group having the formula:



W^1 and W^2 are independently selected at each occurrence from the group: O, S, NH, NHC(=O), C(=O)NH, $NR^{15}C(=O)$, C(=O)NR¹⁵, C(=O), C(=O)O, OC(=O), NHC(=S)NH, NHC(=O)NH, SO₂, SO₂NH, -(OCH₂CH₂)₇₆₋₈₄, (OCH₂CH₂)_s, (CH₂CH₂O)_{s'}, (OCH₂CH₂CH₂)_{s''}, (CH₂CH₂CH₂O)_t, and (aa)_{t'};

aa is independently at each occurrence an amino acid;

Z is selected from the group: aryl substituted with 0-3 R¹⁶, C₃₋₁₀ cycloalkyl substituted with 0-3 R¹⁶, and a 5-10 membered heterocyclic ring system containing 1-4 heteroatoms independently selected from N, S, and O and substituted with 0-3 R¹⁶;

R¹³, R^{13a}, R¹⁴, R^{14a}, and R¹⁵ are independently selected at each occurrence from the group: H, =O, COOH, SO₃H, PO₃H, C₁₋₅ alkyl substituted with 0-3 R¹⁶, aryl substituted with 0-3 R¹⁶, benzyl substituted with 0-3 R¹⁶, and C₁₋₅ alkoxy substituted with 0-3 R¹⁶, NHC(=O)R¹⁷, C(=O)NHR¹⁷, NHC(=O)NHR¹⁷, NHR¹⁷, R¹⁷, and a bond to C_h Ch ;

R¹⁶ is independently selected at each occurrence from the group: a bond to C_h , COOR¹⁷, C(=O)NHR¹⁷, NHC(=O)R¹⁷, OH, NHR¹⁷, SO₃H, PO₃H, -OPO₃H₂, -OSO₃H, aryl substituted with 0-3 R¹⁷, C₁₋₅ alkyl substituted with 0-1 R¹⁸, C₁₋₅ alkoxy substituted with 0-1 R¹⁸, and a 5-10 membered heterocyclic ring system containing 1-4 heteroatoms independently selected from N, S, and O and substituted with 0-3 R¹⁷;

R¹⁷ is independently selected at each occurrence from the group: H, alkyl substituted with 0-1 R¹⁸, aryl substituted with 0-1 R¹⁸, a 5-10 membered heterocyclic ring system containing 1-4 heteroatoms independently selected from N, S, and O and substituted with 0-1 R¹⁸, C₃₋₁₀ cycloalkyl substituted with 0-1 R¹⁸, polyalkylene glycol substituted with 0-1 R¹⁸, carbohydrate substituted with 0-1 R¹⁸,

cyclodextrin substituted with 0-1 R^{18} , amino acid substituted with 0-1 R^{18} , polycarboxyalkyl substituted with 0-1 R^{18} , polyazaalkyl substituted with 0-1 R^{18} , peptide substituted with 0-1 R^{18} , wherein the peptide is comprised of 2-10 amino acids, 3,6-O-disulfo-B-D-galactopyranosyl, bis(phosphonomethyl)glycine, and a bond to $C_h Ch$;

R^{18} is a bond to $C_h Ch$;

k is selected from 0, 1, and 2;

h is selected from 0, 1, and 2;

h' is selected from 0, 1, and 2;

g is selected from 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, and 10;

g' is selected from 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, and 10;

s is selected from 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, and 10;

s' is selected from 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, and 10;

s'' is selected from 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, and 10;

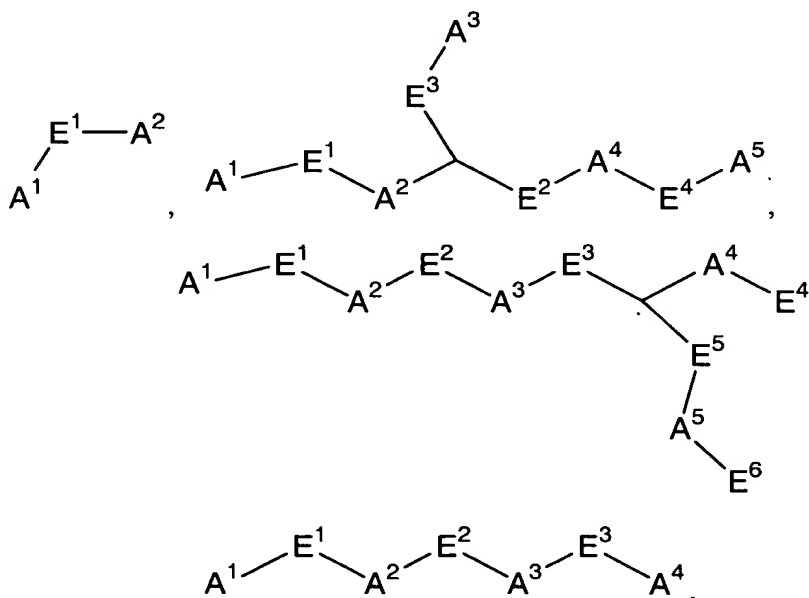
t is selected from 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, and 10;

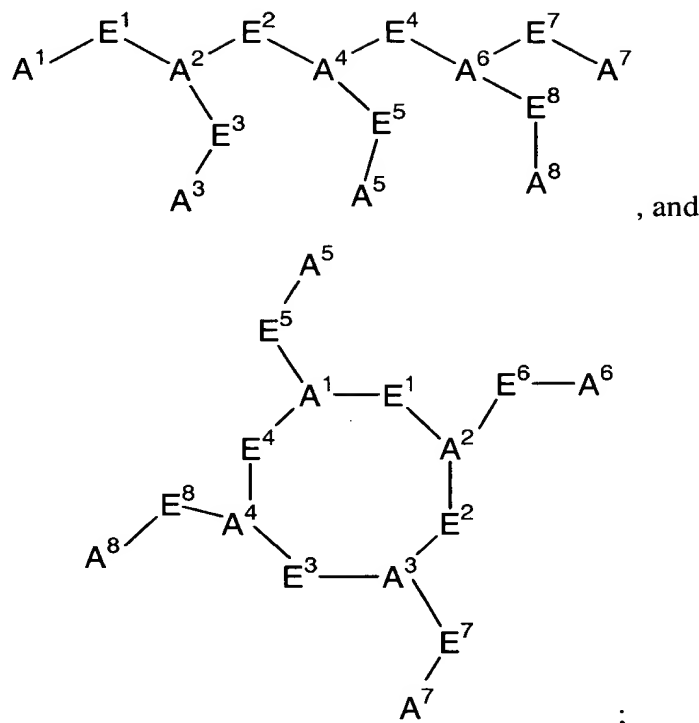
t' is selected from 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, and 10;

x is selected from 0, 1, 2, 3, 4, and 5;

x' is selected from 0, 1, 2, 3, 4, and 5;

$C_h Ch$ is a metal bonding unit having a formula selected from the group:





A¹, A², A³, A⁴, A⁵, A⁶, A⁷, and A⁸ are independently selected at each occurrence from the group: N, NR²⁶, NR¹⁹, NR¹⁹R²⁰, S, SH, -S(Pg), O, OH, PR¹⁹, PR¹⁹R²⁰, -O-P(O)(R²¹)-O-, P(O)R²¹R²², a bond to the targeting moiety and a bond to the linking group;

Pg is a thiol protecting group;

E¹, E², E³, E⁴, E⁵, E⁶, E⁷, and E⁸ are independently a bond, CH, or a spacer group independently selected at each occurrence from the group: C₁-C₁₆ alkyl substituted with 0-3 R²³, aryl substituted with 0-3 R²³, C₃-10 cycloalkyl substituted with 0-3 R²³, heterocyclo-C₁-10 alkyl substituted with 0-3 R²³, wherein the heterocyclo group is a 5-10 membered heterocyclic ring system containing 1-4 heteroatoms independently selected from N, S, and O, C₆-10 aryl-C₁-10 alkyl substituted with 0-3 R²³, C₁-10 alkyl-C₆-10 aryl- substituted with 0-3 R²³, and a 5-10 membered heterocyclic ring system containing 1-4 heteroatoms independently selected from N, S, and O and substituted with 0-3 R²³;

R¹⁹ and R²⁰ are each independently selected from the group: a bond to the linking group, a bond to the targeting moiety, hydrogen, C₁-C₁₀ alkyl substituted with 0-3 R²³, aryl substituted with 0-3 R²³, C₁-₁₀ cycloalkyl substituted with 0-3 R²³, heterocyclo-C₁-₁₀ alkyl substituted with 0-3 R²³, wherein the heterocyclo group is a 5-10 membered heterocyclic ring system containing 1-4 heteroatoms independently selected from N, S, and O, C₆-₁₀ aryl-C₁-₁₀ alkyl substituted with 0-3 R²³, C₁-₁₀ alkyl-C₆-₁₀ aryl- substituted with 0-3 R²³, a 5-10 membered heterocyclic ring system containing 1-4 heteroatoms independently selected from N, S, and O and substituted with 0-3 R²³, and an electron, provided that when one of R¹⁹ or R²⁰ is an electron, then the other is also an electron;

R²¹ and R²² are each independently selected from the group: a bond to the linking group, a bond to the targeting moiety, -OH, C₁-C₁₀ alkyl substituted with 0-3 R²³, C₁-C₁₀ alkyl substituted with 0-3 R²³, aryl substituted with 0-3 R²³, C₃-₁₀ cycloalkyl substituted with 0-3 R²³, heterocyclo-C₁-₁₀ alkyl substituted with 0-3 R²³, wherein the heterocyclo group is a 5-10 membered heterocyclic ring system containing 1-4 heteroatoms independently selected from N, S, and O, C₆-₁₀ aryl-C₁-₁₀ alkyl substituted with 0-3 R²³, C₁-₁₀ alkyl-C₆-₁₀ aryl- substituted with 0-3 R²³, and a 5-10 membered heterocyclic ring system containing 1-4 heteroatoms independently selected from N, S, and O and substituted with 0-3 R²³;

R²³ is independently selected at each occurrence from the group: a bond to the linking group, a bond to the targeting moiety, =O, F, Cl, Br, I, -CF₃, -CN, -CO₂R²⁴, -C(=O)R²⁴, -C(=O)N(R²⁴)₂, -CHO, -CH₂OR²⁴, -OC(=O)R²⁴, -OC(=O)OR^{24a}, -OR²⁴, -OC(=O)N(R²⁴)₂, -NR²⁵C(=O)R²⁴, -NR²⁵C(=O)OR^{24a}, -NR²⁵C(=O)N(R²⁴)₂, -NR²⁵SO₂N(R²⁴)₂, -NR²⁵SO₂R^{24a}, -SO₃H, -SO₂R^{24a}, -SR²⁴, -S(=O)R^{24a}, -SO₂N(R²⁴)₂, -N(R²⁴)₂, -NHC(=S)NHR²⁴, =NOR²⁴, NO₂, -C(=O)NHOR²⁴, -C(=O)NHN(R²⁴)R^{24a}, -OCH₂CO₂H, 2-(1-morpholino)ethoxy, C₁-C₅ alkyl, C₂-C₄ alkenyl, C₃-C₆ cycloalkyl, C₃-C₆ cycloalkylmethyl, C₂-C₆

alkoxyalkyl, aryl substituted with 0-2 R²⁴, and a 5-10 membered heterocyclic ring system containing 1-4 heteroatoms independently selected from N, S, and O; and

wherein at least one of A¹, A², A³, A⁴, A⁵, A⁶, A⁷, A⁸ or R²³ is a bond to the linking group or targeting moiety;

R²⁴, R^{24a}, and R²⁵ are independently selected at each occurrence from the group: a bond to the linking group, a bond to the targeting moiety, H, C₁-C₆ alkyl, phenyl, benzyl, C₁-C₆ alkoxy, halide, nitro, cyano, and trifluoromethyl; and

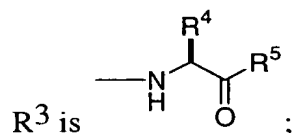
R²⁶ is a co-ordinate bond to a metal or a hydrazine protecting group; or a pharmaceutically acceptable salt thereof.

29. (*currently amended*) A compound according to claim 28 wherein:

R is -OH;

R² is ~~C₁-6 alkyl~~ C₁₋₆ alkyl;

X is C=O;



R¹ and R⁴ are taken together to form a bridging group of formula -(CH₂)₃-O-phenyl-CH₂-; and

R⁵ is ~~NH(C₁-6 alkyl)~~, NH(C₁₋₆ alkyl), substituted with a bond to the linking group or a bond to the chelator.

30. (*currently amended*) A compound according to claim 28 wherein:

R is -OH;

R⁹ is C₁ alkyl substituted with a bond to Ln;

R¹⁰ and R¹¹ taken together with the nitrogen atom to which they are attached form a 5 atom saturated ring system, wherein said ~~right ring~~ ring system is substituted with 0-3 R²⁷;

R²⁷ is =O, ~~C₁-4 alkyl~~ C₁₋₄ alkyl, or phenyl substituted with R²⁸; and

R²⁸ is a phenoxy group substituted with 0-2 OCH₃ groups.

31. (*currently amended*) A compound according to claim 28 wherein

R is -OH;

R¹ and R² taken together with the ~~nitrogen and~~ carbon ~~atom~~ atoms through which they are attached form a C₅₋₇ atom saturated ring system substituted with one or more substituents selected from the group consisting of: a bond to Ln, a bond to Ch, and -C(=O)-NR²⁹R³⁰;

R²⁹ and R³⁰ taken together with the nitrogen atom through which they are attached form a ~~C₅₋₇~~ C₅₋₇ atom saturated ring system substituted with R³¹; and

R³¹ is a benzyloxy group substituted with ~~C₁₋₄ alkyl~~ C₁₋₄ alkyl.

32. (*currently amended*) A compound according to claim 28 wherein

d is selected from 1, 2, 3, 4, and 5;

W¹ and W² are ~~W is~~ independently selected at each occurrence from the group: O, NH, NHC(=O), C(=O)NH, NR¹⁵C(=O), C(=O)NR¹⁵, C(=O), C(=O)O, OC(=O), NHC(=S)NH, NHC(=O)NH, SO₂, (OCH₂CH₂)_s, (CH₂CH₂O)_s', (OCH₂CH₂CH₂)_s'', (CH₂CH₂CH₂O)_t, and (aa)_t';

aa is independently at each occurrence an amino acid;

Z is selected from the group: aryl substituted with 0-1 R¹⁶, C₃₋₁₀ cycloalkyl substituted with 0-1 R¹⁶, and a 5-10 membered heterocyclic ring system containing 1-4 heteroatoms independently selected from N, S, and O and substituted with 0-1 R¹⁶;

R¹³, R^{13a}, R¹⁴, R^{14a}, and R¹⁵ are independently selected at each occurrence from the group: H, =O, COOH, SO₃H, C₁₋₅ alkyl substituted with 0-1 R¹⁶, aryl substituted with 0-1 R¹⁶, benzyl substituted with 0-1 R¹⁶, ~~and~~ C₁₋₅ alkoxy substituted with 0-1 R¹⁶, NHC(=O)R¹⁷, C(=O)NHR¹⁷, NHC(=O)NHR¹⁷, NHR¹⁷, R¹⁷, and a bond to ~~C_h~~ Ch;

k is 0 or 1;
s is selected from 0, 1, 2, 3, 4, and 5;
s' is selected from 0, 1, 2, 3, 4, and 5;
s'' is selected from 0, 1, 2, 3, 4, and 5;
t is selected from 0, 1, 2, 3, 4, and 5;

A¹, A², A³, A⁴, A⁵, A⁶, A⁷, and A⁸ are independently selected at each occurrence from the group: NR¹⁹, NR¹⁹R²⁰, S, SH, OH, and a bond to ~~L_n~~ L_n;

E is a bond, CH, or a spacer group independently selected at each occurrence from the group: C₁-C₁₀ alkyl substituted with 0-3 R²³, aryl substituted with 0-3 R²³, C₃-₁₀ cycloalkyl substituted with 0-3 R²³, and a 5-10 membered heterocyclic ring system containing 1-4 heteroatoms independently selected from N, S, and O and substituted with 0-3 R²³;

R¹⁹, and R²⁰ are each independently selected from the group: a bond to ~~L_n~~ L_n, hydrogen, C₁-C₁₀ alkyl substituted with 0-3 R²³, aryl substituted with 0-3 R²³, a 5-10 membered heterocyclic ring system containing 1-4 heteroatoms independently selected from N, S, and O and substituted with 0-3 R²³, and an electron, provided that when one of R¹⁹ or R²⁰ is an electron, then the other is also an electron;

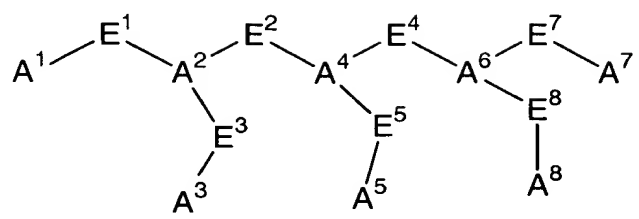
R²³ is independently selected at each occurrence from the group: a bond to ~~L_n~~ L_n, =O, F, Cl, Br, I, -CF₃, -CN, -CO₂R²⁴, -C(=O)R²⁴, -C(=O)N(R²⁴)₂, -CH₂OR²⁴, -OC(=O)R²⁴, -OC(=O)OR^{24a}, -OR²⁴, -OC(=O)N(R²⁴)₂, -NR²⁵C(=O)R²⁴, -NR²⁵C(=O)OR^{24a}, -NR²⁵C(=O)N(R²⁴)₂, -NR²⁵SO₂N(R²⁴)₂, -NR²⁵SO₂R^{24a}, -SO₃H, -SO₂R^{24a}, -S(=O)R^{24a}, -SO₂N(R²⁴)₂, -N(R²⁴)₂, -NHC(=S)NHR²⁴, ~~=NOR¹⁸~~, ~~—C(=O)NHNR¹⁸R^{18a}~~, =NOR²⁴, -C(=O)NHNR²⁴R^{24a}, -OCH₂CO₂H, and 2-(1-morpholino)ethoxy; and

R²⁴, R^{24a}, and R²⁵ are independently selected at each occurrence from the group: a bond to ~~L_n~~ L_n, H, and C₁-C₆ alkyl; ~~and~~.

33. (currently amended) A compound according to claim 28 wherein

d is 1,

Ch Ch is



A¹ is a bond to L_n;

A², A⁴, and A⁶ are each N;

A³, A⁵, A⁷ and A⁸ are each OH;

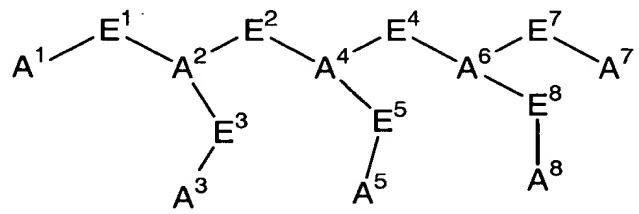
E¹, E², and E⁴ are ~~C₂ alkyl~~ C₂ alkyl;

E³, E⁵, E⁷, and E⁸ are C₂ alkyl substituted with 0-1 R²³; **and**

R²³ is =O_{1/2}.

34. (*currently amended*) A compound according to claim 28 wherein

Ch Ch is



wherein:

A⁵ A⁵ is a bond to L_n;

A¹, A³, A⁷ and A⁸ are each OH;

A², A⁴ and A⁶ are each NH;

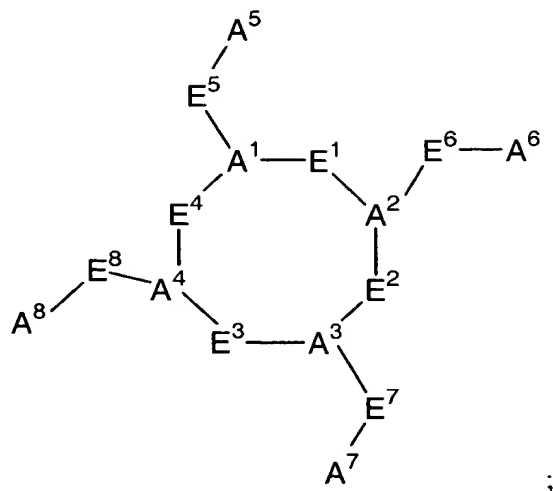
E¹, E³, E⁵, E⁷, and E⁸ are C₂ alkyl substituted with 0-1 R²³;

E², and E⁴, are C₂ alkyl;

R²³ is =O.

35. (*currently amended*) A compound according to claim 28 wherein

Ch is



A¹, A², A³ and A⁴ are each N;

A⁵, A⁶ and A⁸ are each OH;

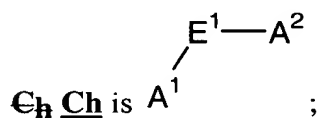
A⁷ is a bond to L_n;

E¹, E², E³, E⁴ are each independently, C₂ alkyl; and

E⁵, E⁶, E⁷, E⁸ are each independently, C₂ alkyl substituted with 0-1 R²³; **and**

R²³ is =O;.

36. (*currently amended*) A compound according to claim 28 wherein



A¹ is NR²⁶;

R²⁶ is a co-ordinate bond to a metal; or a hydrazine protecting group;

E¹ is a bond;

A² is NHR¹⁹;

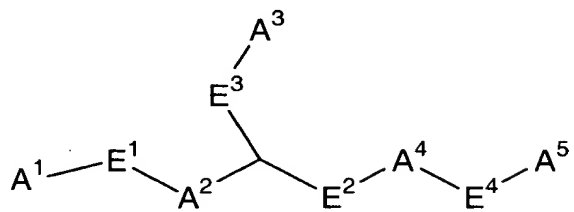
R¹⁹ is a heterocycle substituted with R²³, the heterocycle being selected from pyridine and pyrimidine;

R²³ is selected from a bond to L_n, C(=O)NHR²⁴ and C(=O)R²⁴; and

R²⁴ is a bond to L_n L_n.

37. (*currently amended*) A compound according to claim 28 wherein

Ch is



wherein:

A¹ and A⁵ are each -S(Pg);

Pg is a thiol protecting group;

E¹ and E⁴ are C₂ alkyl substituted with 0-1 R²³;

R²³ is =O;

A² and A⁴ are each -NH;

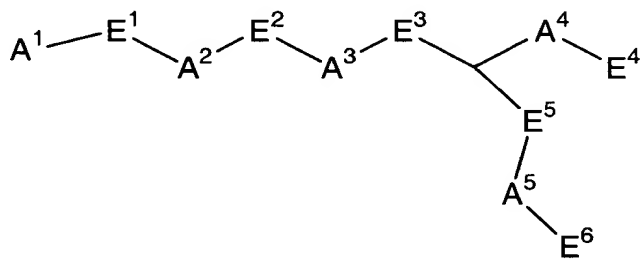
E² is CH₂;

E³ is ~~C1-3 alkyl~~ C₁₋₃ alkyl substituted with 0-1 R²³;

A³ is a bond to Ln.

38. (*currently amended*) A compound according to claim 28 wherein

Ch is



wherein:

A¹ ~~is~~ is a bond to Ln;

E¹ is C₁ alkyl substituted by R²³;

A² is NH;

E² is C₂ alkyl ~~substituted with~~ substituted with 0-1 R²³;

A³ is -O-P(O)(R²¹)-O;

E³ is C₁ alkyl;
A⁴ and A⁵ are each -O-;
E⁴ and E⁶ are each independently C₁₋₁₆ alkyl substituted with 0-1R²³;
E⁵ is C₁ alkyl;
A⁵ is -O-;
R²¹ is -OH; and
R²³ is =O.

39. *(original)* A compound according to claim 28 wherein

W¹ is C(=O)NR¹⁵;
h is 1;
g is 3;
R¹³ and R¹⁴ are independently H;
x is 1;
k is 0;
g' is 0;
h' is 1;
W² is NH; and
x' is 1.

40. *(original)* A compound according to claim 28 wherein

x is 0;
k is 1;
Z is aryl substituted with 0-3 R¹⁶;
g' is 1;
W² is NH;
R^{13a} and R^{14a} are independently H;
h' is 1; and
x' is 1.

41. (*currently amended*) A compound according to claim 28 wherein

W¹ is C(=O)NR¹⁵;

h is 1;

g is 2;

R¹³ and R¹⁴ are independently H;

x is 1;

k is 0;

g' is 1;

R^{13a} and R^{14a} are independently H; or ~~C₁₋₅ alkyl~~ C₁₋₅ alkyl substituted with
0-3 R¹⁶;

R¹⁶ is SO₃H;

W² is NHC(=O) or NH;

h' is 1; and

x' is 2.

42. (*original*) A compound according to claim 28 wherein

W¹ is C(=O)NH;

h is 1;

g is 3;

R¹³ and R¹⁴ are independently H;

k is 0;

g' is 0;

x is 1;

W² is -NH(C=O)- or -(OCH₂CH₂)₇₆₋₈₄;

h' is 2; and

x' is 1.

43. (*original*) A compound according to claim 28 wherein

x is 0;

k is 0;

g' is 3;
h' is 1;
W² is NH; and
x' is 1.

44. (*currently amended*) A compound according to claim 28 wherein
x is 0;
Z is aryl substituted with 0-3 R¹⁶;
k is 1;
g' is 1;
R^{13a} and R^{14a} are independently H;
W² is NHC(=O) or ~~-(OCH₂CH₂)₇₆₋₈₄-~~ -(OCH₂CH₂)₇₆₋₈₄-; and
x' is 1.

45. (*original*) A compound according to claim 28 wherein
W¹ is C=O;
g is 2;
R¹³ and R¹⁴ are independently H;
k is 0;
g' is 0;
h' is 1;
W² is NH; and
x' is 1.

46. (*currently amended*) A compound according to claim 1 selected from the group consisting of:
2-{[5-(3-{2-[(6-Hydroxycarbamoyl-7-isobutyl-8-oxo-2-oxa-9-aza-bicyclo[10.2.2]hexadeca-1(15),12(16),13-triene-10-carbonyl)-amino]-acetylamino}-propylcarbamoyl)-pyridin-2-yl]-hydrazonomethyl}-benzenesulfonic acid;

2-{{[5-(4-{{[(6-Hydroxycarbamoyl-7-isobutyl-8-oxo-2-oxa-9-aza-bicyclo[10.2.2]hexadeca-1(15),12(16),13-triene-10-carbonyl)-amino]-methyl}-benzylcarbamoyl)-pyridin-2-yl]-hydrazonomethyl}-benzenesulfonic acid;

2-[7-({N-[3-(2-{{[7-(N-hydroxycarbamoyl)(3S,6R,7S)-4-aza-6-(2-methylpropyl)-11-oxa-5-oxobicyclo[10.2.2]hexadeca-1(15),12(16),13-trien-3-yl]carbonylamino}acetylaminopropyl]carbamoyl}methyl)-1,4,7,10-tetraaza-4,10-bis(carboxymethyl)cyclododecyl]acetic acid;

2-{7-[(N-{{[4-{{[7-(N-hydroxycarbamoyl)(3S,6R,7S)-4-aza-6-(2-methylpropyl)-11-oxa-5-oxobicyclo[10.2.2]hexadeca-1(15),12(16),13-trien-3-yl]-carbonylamino}methyl)phenyl]methyl}carbamoyl)methyl]-1,4,7,10-tetraaza-4,10-bis(carboxymethyl)cyclododecyl}acetic acid;

2-(7-{{[N-(1-{{N-[3-(2-{{[7-(N-hydroxycarbamoyl)(3S,6R,7S)-4-aza-6-(2-methylpropyl)-11-oxa-5-oxobicyclo[10.2.2]hexadeca-1(15),12(16),13-trien-3-yl]carbonylamino}acetylaminopropyl]carbamoyl}-2-sulfoethyl)carbamoyl]methyl}-1,4,7,10-tetraaza-4,10-bis(carboxymethyl)cyclododecyl}acetic acid;

2-[7-({N-[1-(N-{{[4-{{[7-(N-hydroxycarbamoyl)(3S,6R,7S)-4-aza-6-(2-methylpropyl)-11-oxa-5-oxobicyclo[10.2.2]hexadeca-1(15),12(16),13-trien-3-yl]-carbonylamino}methyl)phenyl]methyl}carbamoyl)-2-sulfoethyl]carbamoyl}methyl)-1,4,7,10-tetraaza-4,10-bis(carboxymethyl)cyclododecyl]acetic acid;

2-((2-(((N-[3-(2-{{[7-(N-hydroxycarbamoyl)(3S,6R,7S)-4-aza-6-(2-methylpropyl)-11-oxa-5-oxobicyclo[10.2.2]hexadeca-1(15),12(16),13-trien-3-yl]carbonylamino}acetylaminopropyl]carbamoyl}methyl)(carboxymethyl)amino}ethyl){2-[bis(carboxymethyl)amino]ethyl}amino}acetic acid;

2-(((2-(((N-[3-(2-{{[7-(N-hydroxycarbamoyl)(3S,6R,7S)-4-aza-6-(2-methylpropyl)-11-oxa-5-oxobicyclo[10.2.2]hexadeca-1(15),12(16),13-trien-3-yl]carbonylamino}acetylaminopropyl]carbamoyl}methyl)(carboxymethyl)]amino}ethyl){2-[bis(carboxymethyl)amino]ethyl}amino}acetic acid;

2-((2-{{[N-{{[4-{{[7-(N-hydroxycarbamoyl)(3S,6R,7S)-4-aza-6-(2-methylpropyl)-11-oxa-5-oxobicyclo[10.2.2]hexadeca-1(15),12(16),13-trien-3-yl]-carbonylamino}methyl)phenyl]methyl}carbamoyl)methyl](carboxymethyl)amino}ethyl){2-[bis(carboxymethyl)amino]ethyl}amino}acetic acid;

N-[3-(2-([7-(N-hydroxycarbamoyl)(3S,6R,7S)-4-aza-6-(2-methylpropyl)-11-oxa-5-oxobicyclo[10.2.2]hexadeca-1(15),12(16),13-trien-3-yl]carbonylamino} acetylaminopropyl)-4,5-bis[2-(ethoxyethylthio)acetylaminopentanamide;

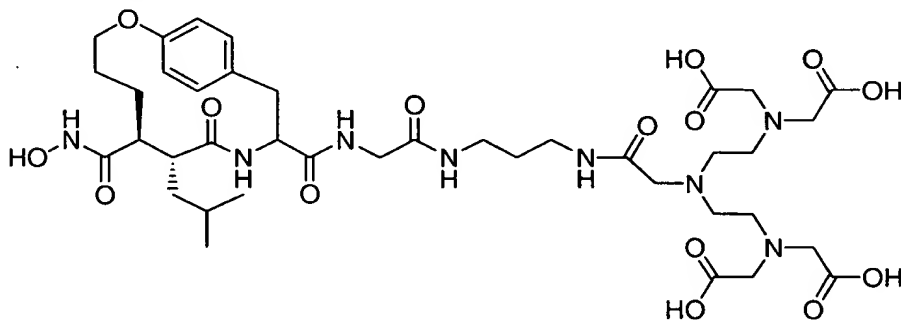
N-{[4-([7-(N-hydroxycarbamoyl)(3S,6R,7S)-4-aza-6-(2-methylpropyl)-11-oxa-5-oxobicyclo[10.2.2]hexadeca-1(15),12(16),13-trien-3-yl]carbonylamino} methyl)-phenyl]methyl}-4,5-bis[2-(ethoxyethylthio)acetylaminopentanamide;

1-(1,2-Dipalmitoyl-sn-glycero-3-phosphoethanolamino)- α,ω -dicarbonylPEG3400-2-([7-(N-hydroxycarbamoyl)(3S,6R,7S)-4-aza-6-(2-methylpropyl)-11-oxa-5-oxobicyclo[10.2.2]hexadeca-1(15),12(16),13-trien-3-yl]carbonylamino)-N-(3-aminopropyl)acetamide;

1-(1,2-Dipalmitoyl-sn-glycero-3-phosphoethanolamino)- α,ω -dicarbonylPEG3400-[7-(N-hydroxycarbamoyl)(3S,6R,7S)-4-aza-6-(2-methylpropyl)-11-oxa-5-oxobicyclo[10.2.2]hexadeca-1(15),12(16),13-trien-3-yl]-N-{[4-(aminomethyl)phenyl]methyl}carboxamide conjugate;

2-[2-([5-[N-(5-(N-hydroxycarbamoyl)(5R)-5-{3-[4-(3,4-dimethoxyphenoxy)phenyl]-3-methyl-2-oxopyrrolidinyl}pentyl)carbamoyl](2-pyridyl))amino)(1Z)-2-azavinyl]benzenesulfonic acid;

2-(2-([5-(N-{3-[3-(N-hydroxycarbamoyl)(4S)-4-([4-(4-methylphenyl)methoxy]piperidyl)carbonyl]piperidyl]-3-oxopropyl}carbamoyl)(2-pyridyl))amino)(1Z)-2-azavinyl]benzenesulfonic acid; and



47. (*original*) A radiopharmaceutical comprising a compound of claim 1 and a cytotoxic radioisotope which is complexed to the chelator.

48. (*original*) A radiopharmaceutical comprising a compound of claim 28 and a cytotoxic radioisotope which is complexed to the chelator.

49. (*original*) A radiopharmaceutical comprising a compound of claim 46 and a cytotoxic radioisotope.

50. (*currently amended*) A radiopharmaceutical according to claim ~~49~~ **20**

wherein the compound is selected from the group consisting of:

2-{{5-(3-{2-[(6-Hydroxycarbamoyl-7-isobutyl-8-oxo-2-oxa-9-aza-bicyclo[10.2.2]hexadeca-1(15),12(16),13-triene-10-carbonyl)-amino]-acetylamino}-propylcarbamoyl)-pyridin-2-yl]-hydrazonomethyl}-benzenesulfonic acid; and

2-{{5-(4-{{(6-Hydroxycarbamoyl-7-isobutyl-8-oxo-2-oxa-9-aza-bicyclo[10.2.2]hexadeca-1(15),12(16),13-triene-10-carbonyl)-amino]-methyl}-benzylcarbamoyl)-pyridin-2-yl]-hydrazonomethyl}-benzenesulfonic acid; and

wherein the cytotoxic radioisotope is ^{99m}Tc.

51. (*original*) A radiopharmaceutical according to claim 47 wherein the cytotoxic radioisotope is selected from the group consisting of beta particle emitters, alpha particle emitters, and Auger electron emitters.

52. (*original*) A radiopharmaceutical according to claim 47 wherein the cytotoxic radioisotope is selected from the group consisting of: ¹⁸⁶Re, ¹⁸⁸Re, ¹⁵³Sm, ¹⁶⁶Ho, ¹⁷⁷Lu, ¹⁴⁹Pm, ⁹⁰Y, ²¹²Bi, ¹⁰³Pd, ¹⁰⁹Pd, ¹⁵⁹Gd, ¹⁴⁰La, ¹⁹⁸Au, ¹⁹⁹Au, ¹⁶⁹Yb, ¹⁷⁵Yb, ¹⁶⁵Dy, ¹⁶⁶Dy, ⁶⁷Cu, ¹⁰⁵Rh, ¹¹¹Ag, and ¹⁹²Ir.

53. (*original*) A radiopharmaceutical according to claim 47 wherein the cytotoxic radioisotope is selected from the group consisting of: ¹⁸⁶Re, ¹⁸⁸Re, ¹⁵³Sm, ¹⁶⁶Ho, ¹⁷⁷Lu, ¹⁴⁹Pm, ⁹⁰Y, ²¹²Bi, ¹⁰³Pd, and ¹⁰⁵Rh.

54. *(original)* A radiopharmaceutical according to claim 47 wherein the cytotoxic radioisotope is selected from the group consisting of: ^{186}Re , ^{188}Re , ^{153}Sm , ^{166}Ho , ^{177}Lu , ^{149}Pm , ^{90}Y , and ^{212}Bi .
55. *(original)* A composition comprising a compound of claim 1, or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable carrier.
56. *(currently amended)* A radiopharmaceutical composition comprising a **radiopharmaceutical compound** of claim 47, or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable carrier.
57. *(original)* A radiopharmaceutical composition **comprising: according to claim 56, further comprising**
a compound comprising:
i) 1-10 targeting moieties;
ii) a chelator; and
iii) 0-1 linking groups between the targeting moiety and chelator;
wherein the targeting moiety is a matrix metalloproteinase inhibitor; and
wherein the chelator is capable of conjugating to a cytotoxic radioisotope;
a cytotoxic radioisotope which is complexed to the chelator;
a pharmaceutically acceptable carrier; and
at least one agent selected from the group consisting of a chemotherapeutic agent and a radiosensitizer agent, or a pharmaceutically acceptable salt thereof.
58. *(original)* A radiopharmaceutical composition according to claim 57, wherein the chemotherapeutic agent is selected from the group consisting of mitomycin, tretinoin, ribomustin, gemcitabine, vincristine, etoposide, cladribine, mitobronitol, methotrexate, doxorubicin, carboquone, pentostatin, nitracrine, zinostatin, cetorelix, letrozole, raltitrexed, daunorubicin, fadrozole, fotemustine, thymalfasin, sobuzoxane, nedaplatin, cytarabine, bicalutamide, vinorelbine, vesnarinone, aminoglutethimide, amsacrine, proglumide, elliptinium acetate, ketanserin, doxifluridine, etretinate,

isotretinoin, streptozocin, nimustine, vindesine, flutamide, drogenil, butocin, carmofur, razoxane, sizofilan, carboplatin, mitolactol, tegafur, ifosfamide, prednimustine, picibanil, levamisole, teniposide, improsulfan, enocitabine, lisuride, oxymetholone, tamoxifen, progesterone, mepitiostane, epitio stanol, formestane, interferon-alpha, interferon-2 alpha, interferon-beta, interferon-gamma, colony stimulating factor-1, colony stimulating factor-2, denileukin diftitox, interleukin-2, and leutinizing hormone releasing factor.

59. *(currently amended)* A radiopharmaceutical composition according to claim 57, wherein said radiosensitizer agent is selected from the group consisting consisting of 2-(3-nitro-1,2,4-triazol-1-yl)-N-(2-methoxyethyl)acetamide, N-(3-nitro-4-quinolinyl)-4-morpholine carboxamidine, 3-amino-1,2,4-benzotriazine-1,4-dioxide, N-(2-hydroxyethyl)-2-nitroimidazole-1-acetamide, 1-(2-nitroimidazol-1-yl)-3-(1-piperidinyl)-2-propanol, and 1-(2-nitro-1-imidazolyl)-3-(1-aziridino)-2-propanol.
60. *(original)* A kit comprising a compound of Claim 1, or a pharmaceutically acceptable salt form thereof and a pharmaceutically acceptable carrier.
61. *(currently amended)* A radiopharmaceutical kit comprising a radiopharmaceutical compound of Claim 47, or a pharmaceutically acceptable salt form thereof and a pharmaceutically acceptable carrier.
62. *(original)* A kit of Claim 60 further comprising a stabilizer.
63. *(original)* A radiopharmaceutical kit according to Claim 61, wherein the radioisotope is ^{186}Re or ^{188}Re and the kit further comprises one or more ancillary ligands and a reducing agent.
64. *(original)* A radiopharmaceutical kit according to Claim 63, wherein the ancillary ligands are tricine and a phosphine.

65. *(currently amended)* A kit comprising: according to claim 60, further comprising
and a compound comprising:

i) 1-10 targeting moieties;

ii) a chelator; and

iii) 0-1 linking groups between the targeting moiety and chelator;

wherein the targeting moiety is a matrix metalloproteinase inhibitor; and

wherein the chelator is capable of conjugating to a cytotoxic radioisotope;

at least one agent selected from the group consisting of a chemotherapeutic agent and a radiosensitizer agent, or a pharmaceutically acceptable salt thereof, and
a pharmaceutically acceptable carrier.

66. *(original)* A kit according to Claim 65, wherein the chemotherapeutic agent is selected from the group consisting of mitomycin, tretinoin, ribomustin, gemcitabine, vincristine, etoposide, cladribine, mitobronitol, methotrexate, doxorubicin, carboquone, pentostatin, nitracrine, zinostatin, cetorelix, letrozole, raltitrexed, daunorubicin, fadrozole, fotemustine, thymalfasin, sobuzoxane, nedaplatin, cytarabine, bicalutamide, vinorelbine, vesnarinone, aminoglutethimide, amsacrine, proglumide, elliptinium acetate, ketanserin, doxifluridine, etretinate, isotretinoin, streptozocin, nimustine, vindesine, flutamide, drogenil, butocin, carmofur, razoxane, sizofilan, carboplatin, mitolactol, tegafur, ifosfamide, prednimustine, picibanil, levamisole, teniposide, improsulfan, enocitabine, lisuride, oxymetholone, tamoxifen, progesterone, mepitiostane, epitio stanol, formestane, interferon-alpha, interferon-2 alpha, interferon-beta, interferon-gamma, colony stimulating factor-1, colony stimulating factor-2, denileukin diftotox, interleukin-2, and leutinizing hormone releasing factor.

67. *(currently amended)* A kit according to Claim 65, wherein radiosensitizer agent is selected from the group ~~consisting~~ consisting of 2-(3-nitro-1,2,4-triazol-1-yl)-N-(2-methoxyethyl)acetamide, N-(3-nitro-4-quinolinyl)-4-morpholinecarboxamidine, 3-amino-1,2,4-benzotriazine-1,4-dioxide, N-(2-hydroxyethyl)-2-nitroimidazole-1-

acetamide, 1-(2-nitroimidazol-1-yl)-3-(1-piperidinyl)-2-propanol, and 1-(2-nitro-1-imidazolyl)-3-(1-aziridino)-2-propanol.

68. *(currently amended)* A method of treating a pathological disorder mediated by a matrix metalloproteinase in a patient which comprises ~~administering~~ administering to a patient in need thereof a therapeutically effective amount of a radiopharmaceutical according to claim 47, and a pharmaceutically acceptable carrier.
69. *(original)* A method of claim 68, wherein the disorder is selected from the group consisting of atherosclerosis, restenosis, angiogenesis, tumor metastasis, tumor growth, osteoarthritis, and rheumatoid arthritis.
70. *(currently amended)* A method of claim 68, wherein the disorder is age related macular degeneration, diabetic retinopathy, proliferative vitreoretinopathy, retinopathy ~~vitreoretinopathy, retinopathy~~ of prematurity, ocular tumors, ocular angiogenesis/neovascularization or ~~and~~ corneal graft rejection.
71. *(original)* A method of claim 68, wherein the disorder is cancer selected from the group consisting of prostate, breast, colon, lung melanoma and lymph cancer.
72. *(original)* A method of inhibiting proliferation of cancer cells, comprising contacting the cancer cells with a proliferation-inhibitory amount of a radiopharmaceutical of claim 47.
73. *(currently amended)* A method of claim 68, wherein the matrix metalloproteinase is selected from the group ~~consisting~~ consisting of: MMP-1, MMP-2, MMP-3, MMP-9, and MMP-14.
74. *(currently amended)* A method of claim 68 wherein the matrix metalloproteinase is selected from the group ~~consisting~~ consisting of: MMP-2, MMP-9, and MMP-14.

75. *(original)* A method of treating cancer in a patient comprising: administering to a patient in need thereof a therapeutic radiopharmaceutical of claim 47 or a pharmaceutically acceptable salt thereof, and at least one agent selected from the group consisting of a chemotherapeutic agent and a radiosensitizer agent, or a pharmaceutically acceptable salt thereof.
76. *(original)* A method according to claim 75 wherein the chemotherapeutic agent is selected from the group consisting of mitomycin, tretinoin, ribomustin, gemcitabine, vincristine, etoposide, cladribine, mitobronitol, methotrexate, doxorubicin, carboquone, pentostatin, nitracrine, zinostatin, cetorelix, letrozole, raltitrexed, daunorubicin, fadrozole, fotemustine, thymalfasin, sobuzoxane, nedaplatin, cytarabine, bicalutamide, vinorelbine, vesnarinone, aminoglutethimide, amsacrine, proglumide, elliptinium acetate, ketanserin, doxifluridine, etretinate, isotretinoin, streptozocin, nimustine, vindesine, flutamide, drogenil, butocin, carmofur, razoxane, sizofilan, carboplatin, mitolactol, tegafur, ifosfamide, prednimustine, picibanil, levamisole, teniposide, improsulfan, enocitabine, lisuride, oxymetholone, tamoxifen, progesterone, mepitiostane, epitio stanol, formestane, interferon-alpha, interferon-2 alpha, interferon-beta, interferon-gamma, colony stimulating factor-1, colony stimulating factor-2, denileukin diftotox, interleukin-2, and leutinizing hormone releasing factor.
77. *(currently amended)* A method according to claim 75 wherein the radiosensitizer agent is selected from the group ~~consisting~~ consisting of 2-(3-nitro-1,2,4-triazol-1-yl)-N-(2-methoxyethyl)acetamide, N-(3-nitro-4-quinolinyl)-4-morpholinecarboxamide, 3-amino-1,2,4-benzotriazine-1,4-dioxide, N-(2-hydroxyethyl)-2-nitroimidazole-1-acetamide, 1-(2-nitroimidazol-1-yl)-3-(1-piperidiny)-2-propanol, and 1-(2-nitro-1-imidazolyl)-3-(1-aziridino)-2-propanol.
78. *(original)* A process for the preparation of a radiopharmaceutical, said process comprising generating a macrostructure from a plurality of molecular components

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PATENT

Application No.: 09/783,248

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wherein the plurality of components includes a compound of claim 1 and a cytotoxic radioisotope.

79. *(canceled)*